

# codex alimentarius commission



FOOD AND AGRICULTURE  
ORGANIZATION  
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**Agenda Item 11**

**Conference Room document 4  
(English, French and Spanish)**

## **JOINT FAO/WHO FOOD STANDARDS PROGRAMME**

### **CODEX COMMITTEE ON FOOD HYGIENE**

**Thirty-third Session  
Washington, D.C., USA, October 23-28, 2000**

#### **RISK PROFILE ON ANTIMICROBIAL-RESISTANT BACTERIA IN FOOD Comments by COMISA and International des Epizooties (OIE)**

##### **COMISA**

COMISA would like to thank the Danish delegation for organising this ad hoc meeting. As there was limited time at the meeting to express all opinions in detail, COMISA welcomes the opportunity to comment on certain points contained in Document CX/FH 00/11.

COMISA has now reviewed the above document prepared by the Danish delegation for submission to the CCFH, and wishes to make the following comments for consideration by CCFH prior to finalization.

#### **1. DESCRIPTION OF THE SITUATION**

##### **A. Introduction**

##### **p 1, line 16-17 (Section 1. A, first paragraph, first sentence)**

This first sentence should be challenged. Where are the reference points for this statement?

In setting the stage it is not clear what is meant by "the numbers of foodborne infections in humans caused by antimicrobial-resistant bacteria has increased" in the opening sentence. What are the increased numbers, i.e.

\* are they absolute numbers simply generated by better surveillance programs?

\* an increase in such numbers could actually represent a lower incidence due confounding effects such as an increasing population, etc.?

\* do such numbers reflect a growing population of at risk humans who are elderly or immunocompromised?

Foodborne bacterial infections are not all resistant to antimicrobials as this first paragraph seems to suggest.

Environmental exposure to resistant bacteria and determinants is not mentioned as a risk factor. For example, hospital effluent entering the environment is a known source of antimicrobial resistant pathogens.

**p 1, line 46 (Section 1. B, first paragraph, third sentence)**

“The increasing prevalence of resistance ...” There is a reduced susceptibility to the new classes of drugs but not increased resistance. MICs are increased but are significantly below the breakpoint.

**p.2, line 1 (Section 1.B, first paragraph, fourth sentence)**

This states that “Food animals, ... are the principal reservoir for Salmonella and Campylobacter”.

Recent studies have shown that wild birds are a significant reservoir. These may become carriers as a result of exposure to human sewage effluent and contaminate areas where food animals may ingest resistant bacteria.

**p 2, line 15 (Section 1.B, second paragraph, fourth sentence)**

The statement “In developing countries ... antimicrobial use in humans is also an important source of antimicrobial resistance in these pathogens”.

COMISA believes that there is no justification in singling out “developing countries” since this equally applies to developed countries.

**p 2, line 38 (Section 1. B, fourth paragraph, second sentence)**

“... the use of antimicrobials in hospitals has resulted in increased incidence of nosocomial transmission of multidrug-resistant enterococci ...”

There is no evidence of a decline in human cases of VRE in the U.K. following the ban of 5 growth promoters in the EU (Public Health Laboratory Service U.K. 2000).

Conclusive proof of transfer of resistance determinants from ingested enterococci of food animal origin to human enterococci has yet to be documented. Therefore, while a potential reservoir of resistant genes may exist in the food animal population, inferring that this is definitive source of resistance in human enteric flora may be inappropriate for some foodborne pathogens.

**Pre-harvest, p 3, line 21-22 (Section 1. C, Pre-harvest, Antimicrobial Use, third sentence)**

“Growth promotion use ... is an area of particular public health concern”

Undoubtedly, a hazard exists but a full risk analysis has yet to be performed. It is therefore appropriate to state that the use of growth promoters is a potential public health concern.

Previous surveillance studies, and more recent surveillance programmes such as National Antimicrobial Resistance Monitoring System (NARMS) in the United States, have not shown trends indicating that the more commonly used GP or related compounds are associated with higher resistance frequency in human isolates. In fact, the significant increases have been seen mostly in the (primarily) human-only drugs such as chloramphenicol.

**p 4, line 1 (Section 1. C, Post-harvest, Antimicrobial Use, second paragraph, third sentence)**

“In the developing world, use of antimicrobials in humans also contributes to antimicrobial resistance in Salmonella.”

Surely, this applies equally, if not more so, to the developed countries where over prescribing by medical clinicians has been reported.

**p 4, line 36-37 (Section 2. A, Limited treatment ... pathogens, second paragraph, first sentence)**

In the case of *Vibrio* and *Shigella* infections, these are human not animal sourced. However, poor hygiene may result in food transmission of infection.

The significance of agricultural antibiotics in human disease can also be questioned inferentially by specific examples. Some bacteria, such as *Salmonella*, have much lower rates of resistance than related species such as *Shigella* which are not associated with transfer from animals to humans. Further, *Salmonella* resistance frequencies to co-used compounds have not increased in decades.

*Streptococcus pyogenes* which causes strep throat, has yet to develop resistance to penicillin, which has been used for more than 50 years in humans, and in animals for therapy and growth promotion. Other bacteria such as *Staphylococcus aureus*, have developed considerable resistance to several antibiotics but are not associated with animal to human transfer. The fact that gram-positive active antimicrobials have been safely used for growth in food animals for decades without influencing human pathogen resistance, is indirect but compelling inferential evidence that agricultural growth uses are not likely major sources of problematic resistances that are of major public health concern.

**p 6 line 25 (Section 4, item 4, first sentence)**

“... the use of antibiotics for growth promotion should be prohibited.”

Consumers need to be aware of the WHO principles elucidated in June 2000. WHO has agreed to the fundamentals established by the Swann Report in 1969 and recognises that there is a role for these products in food animals.

Indeed, the negative impact of their prohibition is now becoming clear in Denmark and other EU countries as discussed below.

There is no substantiation for the claim that consumers feel a) use of antibiotics for growth promotion should be prohibited, or that b) that AGPs are used to cover up for less than adequate food animal production practices. Consumer opinions will vary tremendously according to socioeconomic status, country, general education, and knowledge of food animal production systems.

**p 6 line 40 (Section 5, paragraph 1)**

The benefits of growth promoters are lacking in this document. Environmental and animal welfare benefits should be inserted.

Two papers from Denmark have recently been presented. Both Madsen (2000) and Andreasen (2000) representing the Danish Bacon and Meat Council and the State Veterinary Serum Laboratory respectively, discuss the impact of removal of growth promoters on the health and welfare of pig in the 7 to 35 kg liveweight range.

In the paper by Madsen post-weaning mortality increased from 3.2% to 4.2% associated with increased diarrhoea. Daily liveweight gain fell from 422 g/day to 403 g/day and pigs took one week extra to reach 30 kg liveweight. There was a 60% increase in laboratory submissions to the diagnostic laboratory owned by the National Committee for Pigs.

In the paper by Andreasen, the herds in the survey showed that there was a dramatic increase in the quantities of tetracyclines and macrolide used, approximately double the amounts used before growth promoters were removed.

Similar findings are reported in the poultry industry in the U.K. (Ministry of Agriculture, Fisheries and Food 2000) where following the ban of Gram positive growth promoters, there was an increased incidence of necrotic enteritis and a consequent use of the therapeutic amoxycillin to control this disease.

**p 6 line 43 (Section 5, paragraph 1, last sentence)**

“...the benefits of this use may be relatively small”.

This refers to the use of growth promoters in relation to food production costs. The paper by Madsen referred to above shows an economic benefit in growing and finishing pig of up to \$ 2 per pig and in weaners \$ 0.75 per pig. These costs do not take into consideration the negative economic impact of disease and treatment with therapeutic antimicrobials.

In several countries, this overall cost of \$ 2.75 is greater than the return per pig to the producer. Therefore, the economic benefits as well as the health and welfare of animals are considerable and are passed on to the consumer.

**p 7 line 7 (Section 5, paragraph 3)**

This paragraph confuses the terms “risk” and “hazard”. In all cases, the word “risk” should be replaced by “hazard”.

Many dogmatic statements are made about prophylactic and metaphylactic use resulting in an increased use of antimicrobials in food producing animals compared with therapeutic use without providing evidence for these statements. The term “metaphylaxis” has no official status. “group therapy” or “strategic therapy” are more appropriate.

**p 7 line 12 (Section 5, paragraph 3, fourth sentence)**

“The use of antibiotics in food production to enhance growth has greater risks than any therapeutic or prophylactic use in agriculture...”.

This statement is totally without foundation and cannot possibly be accepted in any scientific review of the subject. Recent surveillance by the National Antimicrobial Resistance Monitoring System (NARMS) in the US have not shown trends indicating that growth promoters are associated with higher resistance frequency in human isolates.

As previously discussed above, the impact of the withdrawal of growth enhancers in the EU has had a considerable negative impact and has led to the higher usage of therapeutics.

**p 10 line 28 (Section 7, first bullet)**

On page 10, line 28 replace "...result in an increase.." with "....result in an incremental increase....."

**p 10 line 30 (Section 7, second bullet)**

Replace “risk” by “hazard”

**COMISA POSITION**

Although COMISA has already provided input to this paper there are statements that are contained therein that COMISA wishes to challenge and have discussed in open forum at CCFH.

The complexities of resistance transfer associated with the use of antimicrobials in food animals are such that COMISA supports strongly the final point of the paper under 8. RECOMMENDATIONS, which calls for the CCFH to commission risk assessments for selected specific scenarios relating to antimicrobial-resistant bacteria in food.

Without such risk assessments, it is not possible to fully define the level of risk that may exist where essential antimicrobials are used in livestock production.

The provision of safe, healthy food for the dramatically increasing global population is the prime target of the livestock producer and the judicious use of antimicrobials to ensure healthy food animals remains a high priority.

At the same time, COMISA strongly supports this paper in terms of implementation of food hygiene measures and recommends that ancillary risk assessments are performed to look at the mechanisms such as HACCP in the slaughter process, food handling, cross-contamination in preparation of food and the role of wild birds/rodents and their access to open human sewage operations.

**OIE**

The present message is destined to inform the participants of the 33th Session of the Codex Committee on Food Hygiene about the work undertaken by the OIE in the field of problems linked with antimicrobial resistance. The text mentioned below is a contribution of the OIE to the discussion on document CX/FH00/11 dated August 2000.

The emergence of antimicrobial resistance in human pathogenic bacteria raises a problem of public health. The use of antimicrobials in livestock production has been suspected to contribute to this increased resistance.

As antimicrobials are precious medicinal products for the protection of animal and human health, the International Committee of the Office International des Epizooties (OIE) has considered it to be important to develop an appropriate strategy for the in-depth investigation of this issue.

Acknowledging the importance of risk analysis and the need for standardization and harmonization of laboratory methodologies as well as the programmes monitoring antimicrobial resistance and the use of antimicrobial substances, the OIE International Committee has decided during its 67th General Session (May 1999) to set up an Ad hoc Group and has defined its terms of references which are the following:

1. Development of an appropriate risk analysis methodology for the potential impact on public health of antimicrobial resistant bacteria of animal origin.
2. Development of technical guidelines on prudent use of antimicrobials.
3. Development of technical guidelines on monitoring of the quantities of antibiotics used in animal husbandry.
4. Harmonisation, after gathering the necessary information, of national antimicrobial resistance monitoring programmes in animals and animal derived foods. Elaboration of a priority list of relevant bacteria and antimicrobial substances to be included in resistance monitoring programmes.
5. Standardisation and harmonisation of laboratory methodologies used for the detection and quantification of antimicrobial resistance.
  - 5.1. Collection of information on the procedures used in veterinary laboratories and in clinical biological laboratories in different countries for quantitative and qualitative analysis of bacterial resistance to antibiotics.
  - 5.2. Proposal of standardised protocols for analysing the antibiotic resistance of bacteria isolated from animals or products of animal origin, and notably specific procedures for different bacterial groups.
  - 5.3. Proposal on harmonisation of assays on antibiotics in the veterinary laboratories of OIE Member Countries.
  - 5.4. Formulation of recommendations on the preparation and distribution of resistant bacterial strains taking account of international reference strains and the requirement for biosecurity.

Taking into consideration the responsibility of the OIE as one of the international organisations specially referred to under the Agreement on Sanitary and Phytosanitary Measures of the World Trade Organization (WTO), the recommendations developed by this Ad hoc Group should be practicable and applicable in all OIE Member Countries.

Purpose of the electronic world wide consultation:

Draft documents on each of the five topics were elaborated by the OIE Ad hoc Group on Antimicrobial Resistance. The purpose of this world wide consultation is to solicit comments and suggestions from all parties concerned by the problems of human and animal health associated with the emergence and spread of antimicrobial resistance. This information has, in particular, been addressed to the Chief Veterinary Officers of all OIE Member Countries and to the appropriate structures of the Food and

Agriculture Organization of the United Nations (FAO), the Codex Alimentarius Commission (CAC), the World Trade Organisation (WTO) and the World Health Organisation (WHO). Other structures also addressed are regulatory authorities in charge of authorising the marketing of veterinary medicinal products and organisations representing veterinarians, farmers, physicians, the pharmaceutical industry, the scientific communities and consumers. Comments, suggestions and information is also in particular sought from developing countries.

Guidance for submission of comments and suggestions:

The draft OIE documents and recommendations as well as the comments addressed during this OIE consultation can be accessed on the website of the OIE Collaborating Centre for Veterinary Medicinal Products under the following address: <http://www.anmv.afssa.fr/oiecc/abr>. Contributions should be forwarded by electronic mail to [oie.abr@anmv.afssa.fr](mailto:oie.abr@anmv.afssa.fr) and should be entitled OIE WORLD WIDE PUBLIC CONSULTATION.

Persons sending contributions should indicate their name, professional position, the institution or organisation they are representing.

Contributions should be forwarded separately for each of the five topics. Each contribution should clearly indicate to which of the five topics it relates and for each topic to which paragraph it relates. Contributions should be relevant to the topic and should be as short and concise as possible. Comments on contributions already published on the website are possible and should clearly indicate the name and date of the contribution referred to.

The electronic world wide consultation terminates on 21 September 2000.